

**AMENDMENTS TO THE CLAIMS**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listings of Claims:**

1. (currently amended) A herpes simplex virus vector (HSV vector) comprising: (i) a transcriptional initiation regulatory region of a human calponin gene comprising the nucleotide sequence of Seq. ID No.:1, and (ii) a predetermined gene encoding a transcription factor essential for initiation of a herpes viral replication which is integrated downstream of the transcriptional initiation regulatory region of an ICP4 gene, and further comprising (iii) a thymidine kinase gene[[,]]; wherein the transcriptional initiation regulatory region is integrated upstream from the predetermined gene, and further wherein the HSV vector is not expressed or replicated in normal differentiated cells, wherein the transcriptional initiation regulatory region is a region including the base sequence shown in Seq. ID No. 1 said HSV vector is capable of suppressing its replication at a desired period by using the thymidine kinase gene, and is obtained by the steps comprising: (i) inserting a DNA fragment comprising the transcriptional initiation regulatory region of the human calponin gene into a ribonucleotide reductase gene locus by a homologous recombination; (ii) infecting a virus mixed solution of the homologous recombination to a cell that activates the transcription initiation regulatory region of the human calponin gene or a cell that expresses the human calponin gene; and (iii) purifying said vector to a single clone

without using an agarose overlay assay by using the expression of a gene integrated in the vector as an index.

2. (canceled)

3. (currently amended) The HSV vector according to claim 1, wherein the transcription initiation regulatory region of a human calponin gene including the base nucleotide sequence shown in Seq. ID No. 1 is a region within a human calponin gene promoter comprising a base nucleotide sequence shown in of Seq. ID No. 2.

4. (currently amended) The HSV vector according to claim 3, wherein the region within a human calponin gene promoter including a-base the nucleotide sequence shown in of Seq. ID No. 2 wherein said region within a human calponin gene promoter is a region within a [[base]] nucleotide sequence shown in of Seq. ID No. 3.

5. (canceled)

6. (currently amended) The HSV vector according to any one of claims\_1, 3, or 4, or 5, wherein an enhancer is integrated upstream of the transcriptional initiation regulatory region of a human calponin gene.

7. (currently amended) The HSV vector according to claim 6, wherein the enhancer is a 4F2 enhancer.

8. (currently amended) The HSV vector according to claim 1, wherein a DNA that encodes a desired protein different from the predetermined gene is linked further downstream on the predetermined ICP4 gene, and expresses the desired protein under the control of said transcriptional initiation regulatory region of the ICP4 gene.

9. (currently amended) The HSV vector according to claim 8, wherein the DNA that encodes the desired protein is linked to the predetermined ICP4 gene via an IRES (internal ribosomal entry site[()]).

10. (currently amended) The HSV vector according to claim 1 claim 9, wherein the DNA that encodes the desired protein is an apoptosis promotion-related gene.

11. (currently amended) The HSV vector according to claim 1 claim 9, wherein the DNA that encodes the desired protein is a DNA that encodes a protein having a suppressive action of angiogenesis.

12. (currently amended) The HSV vector according to claim 1 claim 9, wherein the DNA that encodes the desired protein is a DNA that encodes a protein having a suppressive action against cancer metastasis.

13. (currently amended) The HSV vector according to claim 1 claim 9, wherein the DNA that encodes the desired protein is a DNA that encodes a protein having a suppressive action against cancer growth.

14. (canceled)

15. (canceled)

16. (canceled)

17. (canceled)

18. (currently amended) The HSV vector according to claim 1, wherein the vector is tumor cell-specific, proliferating smooth muscle-specific in tumor neovasculature, proliferating smooth muscle-specific in proliferating vascular lesion,

proliferating mesangial cell-specific in glomerulonephritis, or proliferating myofibroblast-specific in fibrosis.

19. (canceled)

20. (currently amended) A method for expression/replication of a gene, protein or a peptide of a vector that is not expressed/replicated in normal differentiated cells, wherein comprising, introducing the HSV vector according to claim 1 is introduced into the cells and tissues of an organism, then expressed and replicatedexpressing and replicating the gene, protein, or protein of the vector.

21. (currently amended) A method for suppressing the expression/replication of a gene, protein or a peptide of [[a]] the HSV vector according to claim 1 comprising, wherein introducing the vector according to claim 1 is introduced into the cells and tissues of an organism, then expressed and replicated, and the expression/replicationexpressing and replicating the gene, protein or peptide of the vector, and suppressing the expression/replication of the vector is suppressed at a later desired period.

22. (currently amended) The method according to claim 21, wherein the suppression of the expression/replication of the HSV vector is a suppression suppressed by using administering antiviral drugs, wherein said antiviral drug is including aciclovir [[and]] or ganciclovir.

23. (currently amended) A method for detecting the *in vivo* distribution of [[a]] the HSV vector according to claim 1, wherein the HSV vector according to claim 1 is introduced into the cells and tissues of an organism, then expressed and replicated, and thymidine kinase activity by said vector is determined.

24. (previously presented) The method according to claim 23, wherein the determination of the thymidine kinase activity is a determination by positron emission tomography using an uracil derivative FIAU labeled with  $^{124}\text{I}$ .

25. (original) The method according to any one of claims 20 to 24, wherein the cells and tissues in the organism are tumor tissues, vascular or lymphatic vessel constriction tissues, nephritic tissues or fibrotic tissues.

26. (currently amended) A therapeutic drug comprising the HSV vector according to claim 1 wherein proliferating smooth muscle cells are targeted.

27. (original) The therapeutic drug according to claim 26, wherein the therapeutic drug is against malignant tumor, fibrosis, proliferating vascular lesion or proliferating glomerulonephritis.

28. (original) The therapeutic drug according to claim 27, wherein the therapeutic drug is against malignant fibrous histiocytoma, gastrointestinal stromal tumor or uterine myoma.

29. (currently amended) A therapeutic method for suppressing fibrosis and malignant tumors, wherein comprising introducing the HSV vector according to claim 1 is introduced into fibrotic tissues, wherein said fibrotic tissue is including lung or[[and]] liver, or malignant tumor tissues, wherein said malignant tumor tissue is including breast cancer, gastric cancer or[[and]] pancreatic cancer, then a replicating the HSV vector thereby selectively disrupting proliferating myofibroblasts, proliferating myofibroblasts is selectively disrupted as a result of replication of the vector, and expression of thereby expressing a gene, protein and [[a]] peptide which promote apoptosis of the myofibroblasts, thereby suppressing fibrosis and malignant tumors.

30. (currently amended) The therapeutic method according to claim 29, wherein the therapy is directed against malignant tumor is leiomyosarcoma, malignant fibrous histiocytoma, gastrointestinal stromal tumor or uterine myoma.

31. (currently amended) A therapeutic method for suppressing proliferating vascular lesions, wherein comprising introducing the HSV vector according to claim 1 is introduced into blood vessel or lymphatic vessel constriction tissues or arteriosclerotic tissues [[and]] or tissues with diabetic retinopathy, then a replicating the HSV vector, thereby selectively disrupting proliferating smooth muscle cells or [[a]] perivascular cells is selectively disrupted as a result of replication of the vector, and expressing expression of a gene, protein or a peptide, thereby suppressing proliferating vascular lesions.

32. (currently amended) A therapeutic method for suppressing proliferating glomerulonephritis, comprising introducing wherein the HSV vector according to claim 1 is introduced into a nephritic tissue, then a replicating the HSV vector, thereby selectively disrupting proliferating mesangial cells is selectively disrupted as a result of replication of the vector, and expressing expression of a gene, protein or a peptide, thereby suppressing proliferating glomerulonephritis.

33. (currently amended) The therapeutic method according to any of claims 29 to 32, wherein the HSV vector is administered to a vein or artery.

34. (currently amended) The therapeutic method according to any of claims 29 to 32, wherein suppressing the expression/replication of the HSV vector is suppressed at a desired period by administering an antiviral drug.

35. (currently amended) A method for producing a HSV vector[],]  
wherein a comprising the steps of:

(a) mixing a solution containing (i) an infected cell that activates the transcription initiation regulatory region of the human calponin gene or a cell that expresses the human calponin gene with a herpes simplex virus vector mixed solution after homologous recombination including the vector according to claim 1 is infected to a cell the transcriptional initiation regulatory region of a gene that expresses cell specifically can be activated or a cell that expresses said gene, that comprises a transcriptional initiation regulatory region of a human calponin gene, (ii) a gene encoding a transcription factor essential for initiation of a herpes viral replication which is integrated downstream of the transcriptional initiation regulatory region of an ICP4 gene , and (iii) a thymidine kinase gene;

(b) inserting said solution into a gene fragment containing the transcriptional initiation regulatory region of the human calponin gene to a ribonucleotide reductase gene locus by homologous recombination[],]; and

(c) purifying the expression of a gene integrated in the vector is used as an index to purify to a single clone by limiting dilution without using agarose overlay assay using the expression of a gene integrated in the HSV vector as an index, wherein said HSV vector is not expressed or replicated in normal differentiated cells and that is capable of suppressing its replication at a desired period by using the thymidine kinase gene.

36. (currently amended) The method for producing the HSV vector according to claim 35, wherein the cell is an ICP4 non-expressing cell.